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RHINOLOGY

Orbital complications:diagnosis of different rhinological causes

Yumiko Matsuba · Ulrich Strassen · Benedikt Hofauer · Murat Bas · Andreas Knopf

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Abstract To evaluate the clinical course of orbital complication using a standardised diagnostic pathway. Seventy-three patients with orbital complications underwent a multimodal diagnostic pathway comprising ENT examination, leucocytes/CRP, CT-/MRI-scanning and disease-related data. Twenty-nine patients suffered from rhinosinusitis, 28 from mucoceles, 13 patients from neoplasms and three patients from rheumatic disorders. Clinical examination diagnosed 60 patients with eyelid swelling, 55 patients with ocular pain, 14 patients with diplopia, 4 patients with exophthalmus, 29 patients with visual field defect and 4 patients with visual loss. The diagnostic pathway identified acute rhinosinusitis with a sensitivity/specificity of 90 %/90 %, mucoceles with 79 %/100 %, neoplasms with 100 %/96 % and granulomatosis with polyangiitis with 100 %/100 %, respectively. All patients left the hospital in good general condition and with regular ocular motility; two patients suffered persistent visual loss. The standardised application of a widely accepted diagnostic pathway reliably distinguishes different causes of orbital complication.

Keywords Orbital complication · Periorbital swelling · Management · Paranasal sinuses · Sinusitis

Y. Matsuba · U. Strassen · B. Hofauer · M. Bas · A. Knopf (✉)
Hals-, Nasen-, Ohrenklinik und Poliklinik, Klinikum rechts der Isar, Technische Universität München, Ismaninger Straße 22, 81675 Munich, Germany
e-mail: a.knopf@lrz.tum.de

Introduction

Orbital complications originating from the paranasal sinuses represent serious diseases that potentially cause functional deficits by ocular muscle or optical nerve impairment. Intracranial disease manifestations may imply life threatening complication. A broad variety of underlying diagnoses exists, comprising inflammatory, neoplastic, rheumatic, or endocrine diseases [1]. Acute rhinosinusitis represents the most frequent cause of orbital involvement in the ear, nose and throat (ENT) medicine [2, 3]. A phase-dependent therapeutic approach comprising antibiotics, corticosteroids, functional endoscopic sinus surgery (FESS), or transfacial procedures is established to preserve intraorbital structures, particularly the optical nerve. In contrast, therapeutic regimens in rheumatic or lymphatic conditions are based on immuno-, chemo- and radiotherapy [4, 5]. Surgical approaches are restricted to histologically evidenced cases to provide immunological trigger effects with a subsequent disease aggravation [6–8]. In addition, corticosteroids, a considerable component of anti-inflammatory treatment of orbital complications in acute rhinosinusitis, can mask lymphatic or rheumatic conditions and prolong time to diagnosis dramatically [9]. Besides lymphatic neoplasms, solid sinonasal malignancies consistently bring about orbital manifestations. Diagnostic and therapeutic concepts in sinonasal malignancy have to achieve the best oncological concept with a minimum of functional loss. Therefore, a rough clinical breakdown has to enable distinction of orbital complication in acute rhinosinusitis from autoimmune or neoplastic conditions to optimise treatment regimens and to reduce patient morbidity. In the daily ENT routine, the differential diagnosis of orbital complication is focused on anamnesis, ENT examination, inflammatory haematology and midfacial CT (computed tomography)-scan. A detailed

assessment of the patient's medical history and endoscopic endonasal examination give a rough breakdown of possible differential diagnoses. The lack of symptom specificity prevents an accurate diagnosis at this point. Patients with acute rhinosinusitis usually report of headache, purulent rhinorrhoea, orbital cellulitis and ocular or facial pain. Mucoceles may cause dull pressure and exophthalmus. In sinonasal malignancy patients frequently suffer from epistaxis, visual deficit, or diplopia, caused by indolent intraorbital masses. Autoimmune disorders can also affect the orbit, resulting in orbital cellulitis or visual deficit with or without signs of acute rhinosinusitis. All underlying conditions may be complicated by bacterial superinfection. Contrast-enhanced midfacial CT/MRI (magnetic resonance imaging) scanning visualises the extent of sinonasal affection and a possible orbital and/or intracranial involvement [10, 11]. However, CT- or MRI-scanning does not per se enable differentiation between malignancies and sinonasal autoimmunity or acute rhinosinusitis. The broad variety of differential diagnoses, the lack of symptom specificity, and the difficult anatomical site require a standardised diagnostic procedure. The objective of this study is to assess the aetiology, clinical presentation and epidemiological characteristics of orbital complications and to evaluate a widely used diagnostic pathway.

Subjects and methods

From January 2005 to August 2012, 73 patients were diagnosed with orbital complications in the Department of Otolaryngology/Head and neck surgery, Technical University Munich. Medical records were subjected to standardised assessment of available disease-related data, including mean age at diagnosis, time to diagnosis, mean disease duration, clinical presentation and therapeutic regimens. A standardised diagnostic pathway was applied to all patients, who routinely underwent ENT examination, midfacial CT-scan and analysis of inflammatory blood parameters. Patients also underwent pre- and postoperative ophthalmologic work-ups that included clinical testing of the visus, visual field and bulbus motility. The assessment of exophthalmus was not corrected by imaging data. A diagnosis of purulent rhinorrhoea gave a rough breakdown of patients potentially suffering from acute rhinosinusitis. Midfacial CT-scan visualised the affected sinuses. Time from first symptom to hospitalisation and the anamnesis of trauma/former FESS divided the cohort into patients with mucoceles and neoplasms (Fig. 1).

Symptomatology was recorded from the first day of inpatient treatment until discharge.

Results

Epidemiology

From January 2005 to August 2012, a total of 73 patients were diagnosed with orbital complications in the department of Otolaryngology/Head and neck surgery, Technical University Munich. Twenty-nine (40 %) patients suffered from acute rhinosinusitis. Mean age at diagnosis was

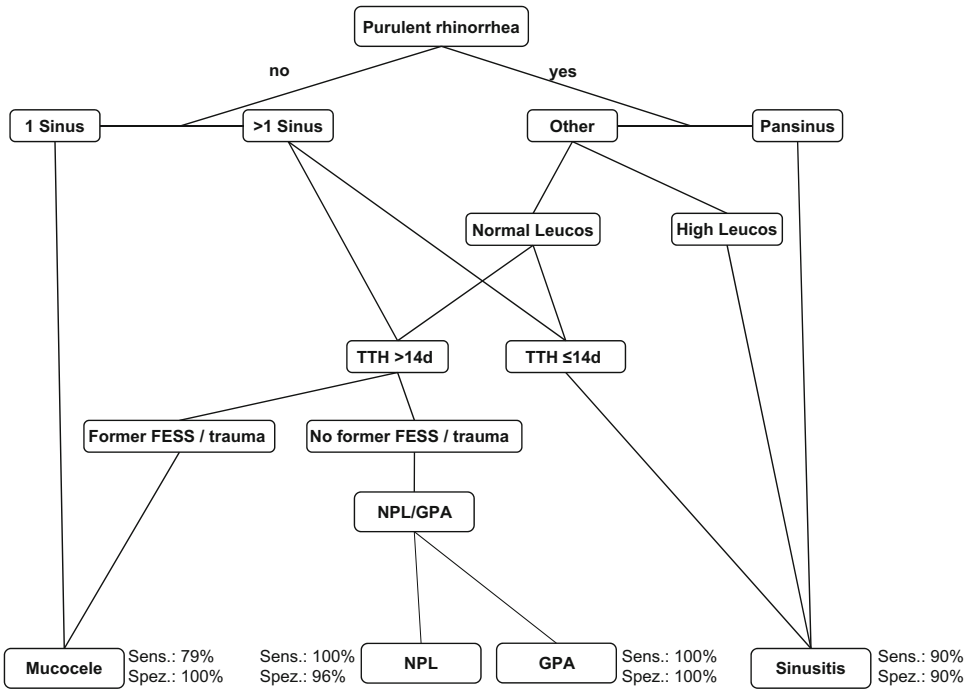

Fig. 1 Diagnostic pathway in orbital complication. *Leucos* leucocytes, *TTH* time to hospitalisation, *NPL* neoplasm

43 years, ranging from 5 to 90 years. There was a slight male preponderance of 1.6:1. Mean disease duration before inpatient treatment was 9.5 days. Twenty-eight (38 %) patients exhibited acute orbital complication caused by mucoceles. Eighteen patients (64 %) developed mucoceles after FESS, six patients (21 %) post-traumatically and four patients (14 %) exhibited spontaneous mucoceles. There was a moderate male predominance of 2.5:1. The mean age at diagnosis was 51 years, ranging from 16 to 89 years. The incidence peaked during the third and fourth decade of life. The mean disease duration before hospitalisation was 99.5 days. Of three patients (4 %) with autoimmune disorders, two (67 %) were diagnosed with granulomatosis with polyangiitis (GPA, Wegener's) and one (33 %) with myasthenia gravis. The mean age at diagnosis was 56 years. The mean disease duration before inpatient treatment was 18.7 days. Thirteen patients (18 %) suffered from neoplastic disorders, comprising 11 (85 %) malignant and two (15 %) benign lesions (Table 1). The mean age of patients with benign disease was 26 years. There were three women and eight men and the mean age was 66 years, ranging from 37 to 91 years. The incidence peaked during the sixth and seventh decades. The mean time before hospitalisation was 105 days. Patients with orbital complications due to sinonasal malignancy were significantly older than patients suffering from mucoceles or acute sinusitis ($p = 0.03$ and $p = 0.009$, respectively). There was no difference between patients with autoimmune disorders and mucoceles or malignancy ($p = 0.66$ and $p = 0.23$, respectively). In addition, the mean time before inpatient treatment was significantly longer in cases of mucocele and sinonasal malignancy compared with acute rhinosinusitis ($p = 0.0002$ and $p = 0.013$, respectively).

Symptomatology

The symptomatology of orbital complications due to rhinological causes is summarised in Table 1. Orbital cellulitis (82 %) and ocular pain (75 %) were the principal symptoms in all differential diagnoses. Patients with acute rhinosinusitis showed the highest rate of diplopia (vs. mucoceles: $p < 0.006$; vs. autoimmune diseases: $p < 0.02$). Exophthalmus and visual loss were infrequent events. Purulent rhinorrhoea was detected in all entities with a significant predominance in acute sinusitis (vs. mucoceles: $p < 0.002$; vs. neoplasms: $p = 0.04$). Recurrent epistaxis occurred exclusively in patients with neoplasms or autoimmune diseases ($p = 0.0009$; $p = 0.001$) (Table 2). Laboratory tests identified significantly elevated leucocytes (11 G/L; reference interval, 4–9 G/L) and C-reactive protein (7 mg/dL; reference interval, <0.5 mg/dL) in acute rhinosinusitis when compared with mucoceles (9 G/L, $p < 0.02$; 3 mg/dL, $p < 0.04$) or neoplasms (7 G/L, $p = 0.01$; 0.3 mg/dL, $p < 0.05$). All patients suffering from GPA tested negative for ANCA (anti-neutrophil cytoplasmatic antibodies) and PR3 (proteinase 3)/MPO (myeloperoxidase). The patient with myasthenia gravis tested positive for acetylcholine receptor antibody (Table 1).

Table 1 Entities and therapeutic regimes

Rhinosinusitis (*n*)	AB therapy (1st line) (*n*)	FESS (*n*)	FESS + TF (*n*)	Hospitalisation (*d*)
Stage I (15)	8	10	0	6.6
Stage II (6)	0	6	0	8.4
Stage III (2)	0	2	0	11.5
Stage IV (6)	0	2	4	10.5
Mucoceles (*n*)	Obliteration	FESS	FESS + TF	Hospitalisation
Frontal (19)	4	3	16	7.6
Ethmoidal (8)	0	8	0	5
Maxillary (1)	0	1	0	3
Tumours (*n*)	Exenteratio	FESS	FESS + TF	Hospitalisation
Osteoma (2)	0	0	2	6.5
Melanoma (3)	0	0	1	14
SCC (4)	1	1	2	13
Adenocarcinoma (1)	0	0	1	6
Adenoidcyst. Ca. (2)	2	0	2	10
NSCLC (1)	0	0	1	5
Autoimmunity (*n*)	AB therapy (1st line)	FESS	FESS + TF	Hospitalisation
GPA (2)	0	2	0	16.5
Myasthenia gravis (1)	1	0	0	4

Table 2 Pre- and post-therapeutic symptomatology

	Sinusitis $N = 29$ pre/post	Mucoceles $N = 28$ pre/post	Neoplasms $N = 13$ pre/post	Autoimmunity $N = 3$ pre/post	All $N = 73/60$ pre/post
Eyelid swelling, *n* (%)	26 (90)/3 (10)	24 (82)/10 (36)	8 (620/na	2 (67)/0	60 (82)/13 (22)
VFD, *n*(%)	22 (76)/0	2 (7)/1 (4)	0/na	0/0	29 (40)/1 (2)
Ocular pain, *n* (%)	25 (86)/0	19 (68)/2 (7)	9 (69)/na	2 (67)/0	55 (75)/2 (3)
MR involvement, *n* (%)	9 (31)/0	0	0/na	1 (33)/0	10 (14)/0
SO involvement, *n* (%)	0/0	1 (4)/0	0/na	0/0	1 (1)/0
SR involvement, *n* (%)	0/0	1 (4)/1 (4)	0/na	0/0	1 (1)/1 (2)
IO involvement, *n* (%)	0/0	0/0	1 (8)/na	1 (33)/0	2 (3)/0
IR involvement, *n* (%)	0/0	0/0	1 (8)/na	1 (33)/0	2 (3)/0
Exophthalmus, *n* (%)	2 (7)/0	0/0	1 (8)/na	1 (33)/0	4 (5)/0
Amaurosis, *n* (%)	1 (3)/1 (3)	0/0	1 (8)/na	0/0	2 (3)/1 (2)
Visual loss, *n* (%)	1 (3)/0	1 (4)/0	0/na	0/0	2 (3)/0
Pur. rhinorrhea, *n* (%)	18 (62)/0	6 (21)/0	4 (31)/2 (15)	1 (33)/0	29 (40)/2 (3)
Epistaxis, *n* (%)	0/0	0/0	1 (8)/0	1 (8)/0	2 (3)/0

VFD visual field defect, *MR* medial rectus, *SO* superior oblique, *SR* superior rectus, *IO* inferior oblique, *IR* inferior rectus, *Pur.* purulent

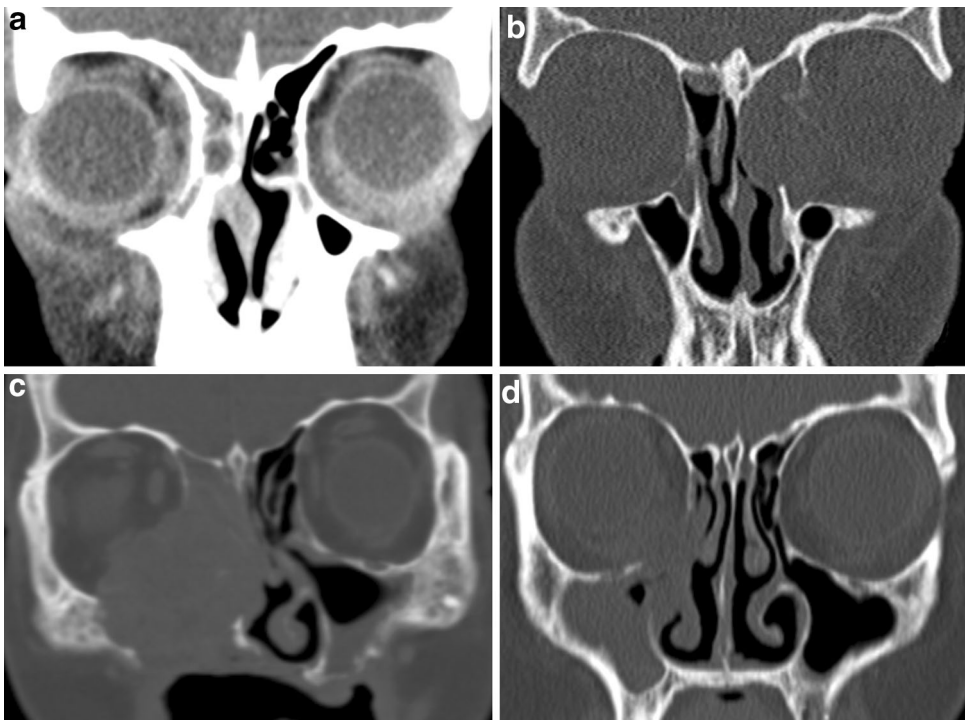

Fig. 2 Coronal CT-scans visualise subperiosteal abscess of the right ethmoid in acute rhinosinusitis (**a**), Mucocele of the left fronto-ethmoidal region that is thinning the lamina papyracea (**b**), carcinoma of the right maxillary sinus that destroys the maxilla and infraorbital margin and shifts up the bulb (**c**), and infiltrating orbital process along the nasolacrimal duct in midfacial GPA (**d**)

CT-/MRI-scan

Midfacial CT-scans were performed in 67/73 (91.7 %) cases. Subsequent MRI-scans were applied to seven patients suspected of orbital/intracranial disease manifestation. Six children underwent primary midfacial MRI. Seventeen patients (59 %) with acute rhinosinusitis showed pansinusitis. Four patients (14 %) suffered from ethmoidal rhinosinusitis, four patients from maxillary rhinosinusitis, three patients (10 %) from frontal rhinosinusitis and one patient (3 %) from sphenoidal rhinosinusitis, respectively. According to Chandler et al. (1970), the majority of patients (52 %) suffered from stage I orbital complication (Table 1) [12]. Subsequent MRI-scanning identified four patients (14 %) with orbital abscess and one patient with an epidural abscess. CT-scan visualised frontal mucoceles in

the majority (68 %) of patients (Table 1). A high proportion of patients with sinonasal malignancy were diagnosed at advanced tumour stages. Fifty percent of our patients demonstrated an infiltration of the orbit and the neurocranium. MRI was conducted in all patients with stage III/IV carcinomas. Both osteomas were found in the frontal sinus. Autoimmune diseases revealed a varying extent of sinus involvement, usually including the maxillary and/or ethmoidal sinus. Pansinus involvement occurred exclusively in acute rhinosinusitis. We observed isolated frontal sinusitis more often in cases of mucocele when compared with acute rhinosinusitis, neoplasms, or autoimmunity ($p < 0.0001$; $p = 0.0006$; $p < 0.04$). There was no difference in the manifestation pattern between malignant neoplasms and autoimmunity (Fig. 2).

Diagnostic pathway and therapy

The diagnostic pathway identified acute rhinosinusitis with a sensitivity and specificity of 90 %. Three patients with stage I orbital complications tested false negative due to a prolonged time to hospitalisation. Detumescent local therapy was applied to all patients. Patients with stage I orbital complications underwent calculated intravenous antibiotic first-line therapy (aminopenicillin/sulbactam or second-generation cephalosporin). Conservative therapy was successful in 8/15 patients (53 %). Subsequent surgical treatment (FESS) were performed when conservative therapy did not lead to symptom resolution within 48 h. FESS and intravenous antibiotic therapy represented first-line therapy in patients with orbital complication stage II–IV. FESS and transfacial surgery was required in four cases with stage IV orbital complication. One patient with stage IV orbital complication underwent combined FESS and transfacial approach due to an intraconal abscess. One patient with stage IV disease was diagnosed with an intracranial abscess. This patient underwent FESS and neurosurgical abscess drainage by a subcranial approach. Patients with ocular muscle or visual deficit were additionally treated with 250 mg prednisolone for 3 days. The mean time of hospitalisation was 9.25 days, ranging from 6.6 (stage I) to 11.5 days (stage III). All patients left our hospital in good general condition and with regular bulbus motility. At discharge, three patients demonstrated a residual eyelid swelling without a compromised visual field. One patient exhibited persistent amaurosis. The diagnostic pathway identified mucoceles with a sensitivity of 79 % and a specificity of 100 %. Six patients tested false negative for mucocele due to bacterial superinfection. All patients with mucoceles with orbital complications underwent primary surgery by FESS and/or transfacial surgery. In four cases frontal sinus obliteration was necessary. The mean hospitalisation time was 5.2 days, ranging 4 days after FESS and 7.6 days after combined surgery. Further surgery was required in three patients due to local recurrence during follow-up. Sinonasal malignancy was diagnosed with a sensitivity/specificity of 100 %/96 %. FESS and transmaxillar/transfrontal surgery were performed in the majority of patients with sinonasal malignancy. Three patients underwent exenteratio orbitae. Adjuvant radiotherapy followed in seven patients. The patient with NSCLC underwent palliative chemotherapy. Patients suffering from frontal osteoma were treated using FESS. The mean hospitalisation time in patients with osteomas was 6 days, in patients with carcinomas 16 days. Malignancy of the sinonasal tract presenting with advanced tumour stages showed local recurrence in 75 % within the first 2 years after surgery. The 5-year survival was 45 %. One patient with preoperative amaurosis exhibited persistent amaurosis after therapy due to an irrecoverable optical nerve impairment. Histological samples were obtained in all surgical approaches. Additional blood tests comprising differential blood count, serum electrophoresis, blood sedimentation rate, auto-antibodies, renal and liver parameters were performed in patients with histological findings suspected for GPA. None of our patients were positive for ANCA/PR3/MPO despite extensive midfacial involvement. Further examinations, e.g. chest CT-scan, abdominal ultrasound and urine sediment excluded systemic disease. After diagnosis, patients with GPA were simultaneously treated with prednisolone (40 mg/day, slowly reduced over 3 months) and methotrexate (15 mg/week). The diagnosis of myasthenia gravis was confirmed by electromyogram and successfully treated with oral corticosteroids. Complete remission was seen in all patients within 6 months (Tables 1, 2).

Discussion

Orbital complications include infectious, neoplastic, inflammatory and posttraumatic conditions. In the present study, clinical signs of orbital involvement were headache, purulent or bloody rhinorrhoea, eyelid swelling, visual deficits, ocular pain, exophthalmia and reduced ocular motility. Concordant with the present literature, acute rhinosinusitis represents the most frequent cause of orbital complication. In our cohort, patients with orbital complication due to acute rhinosinusitis were significantly younger than patients suffering from sinonasal malignancy ($p = 0.03$) or mucoceles ($p = 0.009$). These results match those of other studies that attributed orbital complications to children and adolescents, with an incidence peaking during the first 15 years of age [2, 9]. 73 % of our patients showed an affection of the ethmoid that is held responsible for orbital involvement through dehiscences of its

bony walls or by means of interference with venous drainage of the orbital structures [13]. In contrast to mucoceles and autoimmunity, acute rhinosinusitis frequently causes diplopia, usually stemming from impairment of the musculus rectus medialis ($p < 0.006$; $p < 0.02$). Exophthalmia and visual deficit were infrequently observed. Orbital complication may progress to cavernous sinus thrombophlebitis by infectious spread through the ophthalmic veins. Furthermore, in the presence of orbital involvement there is a higher rate of intracranial spread of infection [14]. The fulminant clinical course of acute rhinosinusitis results in a disease duration of 10 days before inpatient treatment. The immediate diagnosis of acute rhinosinusitis is of major impact to preserve intraocular structures and function. The lack of symptom specificity prompted us to evaluate the performance of a widely used diagnostic pathway comprising anamnesis, ENT endoscopic examination, inflammatory haematology and midfacial CT-scan. It reliably identified orbital complication in acute rhinosinusitis with a sensitivity and specificity of 90 %. Subsequent conservative treatment was indicated in stage I–II orbital complications. When conservative therapy failed to improve symptoms within the first 24–48 h, surgical drainage was mandatory. Subperiosteal abscess was drained via endoscopic ethmoidectomy [15, 16]. Lateral, inferior, or superior abscesses were drained by transfacial ethmoidectomy or a frontal sinus approach [17]. Intracranial expansion required an interdisciplinary subcranial approach. The mean hospitalisation time was 9 days and ranged from 7 (stage I) to 12 days (stage III). All patients left hospital in good general condition and with regular bulbus motility. One patient showed a persistent amaurosis. Some mucoceles become clinically apparent as acute rhinosinusitis because of bacterial superinfection. The diagnostic pathway falsely identified six patients as negative for mucoceles because of bacterial superinfections; hence, diagnostic sensitivity and specificity was 79 and 100 %, respectively. Patients with bacterial superinfection underwent antibiotic treatment and subsequent surgery. Ethmoidal and maxillary mucoceles were successfully treated by FESS. A total of 81 % of the frontal mucoceles were treated by endo- and extranasal sinus surgery. Most authors recommend FESS to prevent scar contraction and stenosis of the nasolacrimal duct caused by transfacial approaches (Janssen-Ritter, Caldwell-Luc) [18, 19]. In contrast, transfacial surgery was required in recurrent mucoceles or laterally situated frontal mucoceles [18–20]. The obliteration of the frontal sinus with abdominal fat is recommended when mucoceles are not accessible endoscopically [21]. A number of publications advocate endoscopic sinus surgery, including the endoscopic-modified Lothrop procedure (also known as Draf III or frontal drillout) as a safe and effective approach for complex and simple paranasal mucocele management [19, 20, 22]. Apart from the common causes of orbital complications it is important to consider rare aetiologies. In our cohort, 22 % of orbital complications refer to sinonasal neoplasms or autoimmunity. Sinonasal malignancy is seen in less than 1 % of all malignant tumours [23]. As found in our study, neoplasms of the sinonasal tract usually occur in the sixth and seventh decades of life. According to present literature, our series identified 81 % of the patients with advanced tumour stages, resulting in intracranial and orbital involvement [24]. While sinus surgery in mucoceles or acute rhinosinusitis focuses on the preservation of intraorbital structures, surgery of sinonasal malignancy aims to reduce patient mortality with a minimum of functional loss. Despite extensive therapeutic approaches, local recurrence was the most frequent treatment failure [25]. Advanced disease stages, aggressive histological subtypes, intracranial and orbital involvement were prognostic factors negatively associated with patient survival. Radical surgery followed by postoperative radiotherapy improves local control and survival when compared with radiotherapy alone [26, 27]. However, the outcome of patients with advanced malignant neoplasm of the sinonasal tract remains poor. The prolonged time to hospitalisation, the affection of several sinuses and the absence of inflammatory haematology all result in a reliable identification of sinonasal malignancy with a diagnostic sensitivity/specificity of 100 %/96 %.

In contrast, advanced midfacial impairment due to GPA is often misinterpreted as sinonasal malignancy or acute rhinosinusitis. Vast heterogeneity in clinical presentation exists, ranging from mild conjunctivitis and episcleritis to more severe inflammation with keratitis, scleritis, uveitis, or retinal vasculitis. It is reported that 8 % of patients with orbital involvement of GPA suffer from vision loss caused by optical nerve compression or granulomatous infiltration [28–31]. Four percent of our patients suffered from sinonasal rheumatic disorders, including two patients with GPA and one patient with myasthenia gravis. The broad variety of symptoms, the lack of symptom specificity and ANCA-negativity highlight the analysis of endonasal biopsies as the diagnostic gold standard [4, 32]. In our cohort, rheumatic disorders were diagnosed by extensive biopsy in two of three cases. One patient underwent FESS and antibiotic first-line therapy due to an acute bacterial superinfection. The low incidence of sinonasal autoimmunity and the broad symptom overlap with acute rhinosinusitis demonstrating that the prevention of intraocular impairment is more important than the potential inflammatory trigger function of FESS in rheumatic conditions [32, 33]. In GPA, therapeutic regimens range from cotrimoxazole treatment to systemic therapy with cyclophosphamide or rituximab

[34–36]. In our cohort, all patients demonstrated complete remission without functional deficit in the follow-up.

Conclusion

Eyelid swelling and ocular pain represent the leading symptoms of orbital complications. The widely accepted diagnostic pathway identified acute rhinosinusitis with a sensitivity/specificity of 90 %/90 %, mucoceles with 79 %/100 %, neoplasms with 100 %/96 % and GPA with 100 %/100 %. Of all patients with benign sinonasal lesions, 98 % left the hospital in good clinical condition and without functional deficit. The mean hospitalisation time ranged from 3 days for patients with mucoceles to 14 days for patients with malignancies.

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Conflict of interest The authors declare no conflict of interest.

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